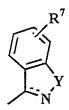
## **CLAIMS**

## 1. A compounds of formula (I)

wherein R1 and R2, which may be the same or different, are each  $C_{2-14}$ heteroaryl,  $C_{6-12}$ aryl $C_{1-6}$ alkyl, C<sub>6-12</sub>aryl, from selected C2-14heteroarylC1-6alkyl (where the alkyl, aryl or heteroaryl moiety may be optionally substituted by one or more substituents selected from C<sub>1-6</sub>alkyl, C<sub>3-6</sub>cycloalkyl, C<sub>4-6</sub>cycloalkenyl, C<sub>6-12</sub>aryl, C<sub>1-6</sub>alkoxy, C<sub>2-14</sub>heteroaryl, halogen, amino, hydroxy, haloC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkylthio, sulphonamide, C<sub>1-6</sub>alkylsulphonyl, hydroxy-C<sub>1-6</sub>alkyl, C<sub>1-s</sub>alkoxycarbonyl, carboxyl, carboxyC<sub>1-s</sub>alkyl, carboxamide and C<sub>3-6</sub>cycloalkyl, C<sub>1-6</sub>alkylcarboxamide), hydrogen, C<sub>1-6</sub>alkyl,  $C_{4-6}$ cycloalkenyl,  $C_{2-6}$ alkenyl,  $C_{2-6}$ alkynyl and  $C_{1-6}$ alkoxy $C_{1-6}$ alkyl (where the alkyl, cycloalkyl, cycloalkenyl, alkenyl, alkynyl, or alkoxyalkyl moieties may be optionally substituted by one or more substituents halogen, hydroxy, C<sub>1-6</sub>alkylcarboxamide, amino. from selected carboxamide, carboxy, C<sub>1-s</sub>alkoxycarbonyl, C<sub>1-s</sub>alkylcarboxy and carboxyC<sub>1-6</sub>alkyl) or one of R<sup>1</sup> and R<sup>2</sup> are as hereinbefore defined and one is hydroxy;

R3 and R4, which may be the same or different, are each selected from  $C_{6-12}$ aryl,  $C_{2-14}$ heteroaryl,  $C_{6-12}$ aryl $C_{1-6}$ alkyl,  $C_{2-14}$ heteroaryl $C_{1-6}$ alkyl (where the alkyl, aryl or heteroaryl moiety may be optionally substituted by one or more substituents selected from  $C_{1\text{-}6}$ alkoxy,  $C_{1-6}$ alkyl,  $C_{3-6}$ cycloalkyl,  $C_{4-6}$ cycloalkenyl,  $C_{6-12}$ aryl,  $C_{2-14}$ heteroaryl, C<sub>1-6</sub>alkylthio, nitro, hydroxy, haloC<sub>1-6</sub>alkyl, amino. halogen, sulphonamide, C<sub>1-6</sub>alkylsulphonyl, hydroxyC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkoxycarbonyl, carboxyl, carboxyC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkylcarboxamide and carboxamide), C<sub>3-6</sub>cycloalkylC<sub>1-6</sub>alkyl, C<sub>3-6</sub>cycloalkyl, C<sub>1-6</sub>alkyl, hydrogen,  $C_{4-6}$ cycloalkenyl,  $C_{2-6}$ alkenyl,  $C_{2-6}$ alkynyl,  $C_{1-6}$ alkoxy- $C_{1-6}$ alkyl, halo haloC<sub>2-6</sub>alkynyl, cyano, haloC<sub>2-6</sub>alkenyl, C<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkylcarboxy and carboxyC<sub>1-6</sub>alkyl (where the alkyl, cycloalkyl, cycloalkenyl, alkenyl, alkynyl, or alkoxyalkyl moieties may be optionally substituted by one or more substituents selected from amino, hydroxy, C<sub>1-6</sub>alkylcarboxamide, carboxamide, carboxy, C<sub>1-6</sub>alkoxycarbonyl, C<sub>1-6</sub>alkylcarboxy and carboxyC<sub>1-6</sub>alkyl); or one of R<sup>3</sup> or R<sup>4</sup> together with one of R<sup>1</sup> or R<sup>2</sup> and the N atom to which it is attached form a 5- or 6-membered heterocyclic ring.

R<sup>5</sup> represents one or more ring substituents selected from halogen, hydrogen C<sub>1-6</sub>alkyl and C<sub>1-6</sub>alkoxy; and R<sup>6</sup> represents a single ring substituent of formula:



wherein the dotted line represents an optional bond; Y is oxygen or - NR<sup>8</sup>

(where  $R^8$  is hydrogen or  $C_{1-6}$ alkyl ) and  $R^7$  represents one or more substituents selected from hydrogen, halogen, halo $C_{1-6}$ alkyl,  $C_{1-6}$ alkyl and  $C_{1-6}$ alkoxy; or

a pharmaceutically acceptable salt or solvate thereof.

A compound according to claim 1 wherein R1 and R2, which may be the 2. same or different, are each independently selected from C6-12 aryl,  $C_{2-14}$ heteroaryl,  $C_{6-12}$ aryl $C_{1-6}$ alkyl,  $C_{2-14}$ heteroaryl $C_{1-6}$ alkyl (where the alkyl, aryl or heteroaryl moiety may be optionally substituted by one or more substituents selected from C<sub>1-6</sub>alkoxy, C<sub>1-6</sub>alkyl, C<sub>3-6</sub>cycloalkyl, C4-6cycloalkenyl, C6-12aryl, C2-14heteroaryl, halogen, amino, hydroxy, haloC<sub>1-6</sub>alkyl, nitro, C<sub>1-6</sub>alkylthio, sulphonamide, C<sub>1-6</sub>alkylsulphonyl, carboxy-C<sub>1-6</sub>alky, carboxamide carboxyl, hydroxyC<sub>1-6</sub>alkyl, C<sub>1-6</sub>alkylcarboxamide), C<sub>1-6</sub>alkyl, C<sub>3-6</sub>cycloalkyl, hydrogen, C<sub>4-6</sub>cycloalkenyl, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl and C<sub>1-6</sub>alkoxyC<sub>1-6</sub>alkyl (where the alkyl, cycloalkyl, cycloalkenyl, alkynyl, or alkoxyalkyl moieties may be optionally substituted by one or more substituents selected from amino, hydroxy, C<sub>1-s</sub>alkylcarboxamide, carboxamide, carboxy and carboxyC<sub>1-6</sub>alkyl) or one of R<sup>1</sup> and R<sup>2</sup> are as hereinbefore defined and one is hydroxy;

 $R^3$  and  $R^4$ , which may be the same or different, are each independently selected from  $C_{6-12}$ aryl,  $C_{2-14}$ heteroaryl,  $C_{6-12}$ aryl $C_{1-6}$ alkyl,

C2-14heteroaryl-C1-6alkyl (where the alkyl, aryl or heteroaryl moiety may be optionally substituted by one or more substituents selected from C<sub>3-6</sub>cycloalkyl, C4-acycloalkenyl, C<sub>1-6</sub>alkoxy, C₁-salkyl, hydroxy, haloC<sub>1-6</sub>alkyl, halogen, amino, C214heteroaryl, C<sub>1-6</sub>alkylthio, sulphonamide, C<sub>1-6</sub>alkylsulphonyl, carboxamide and C<sub>1-6</sub>alkylcarboxamide), hydrogen, C<sub>1-s</sub>alkyl, C<sub>3-6</sub>cycloalkyl.  $C_{4-6}$ cycloalkenyl,  $C_{2-6}$ alkenyl,  $C_{2-6}$ alkynyl,  $C_{1-6}$ alkoxy $C_{1-6}$ alkyl, cyano. carboxyl and carboxyC<sub>1-6</sub>alkyl;

 $R^{5}$  represents one or more ring substituents selected from halogen, hydrogen,  $C_{1\text{-}6}alkyl$  and  $C_{1\text{-}6}alkoxy;$  and

R<sup>6</sup> represents a single ring substituent of formula:

wherein the dotted line represents an optional bond; Y is oxygen or - NR $^8$  (where R $^8$  is hydrogen or C<sub>1-6</sub>alkyl ) and R $^7$  is hydrogen, halogen, C<sub>1-6</sub>alkyl or C<sub>1-6</sub>alkoxy; or a pharmaceutically acceptable salt or solvate thereof.

- 3. A compound according to claim 1 or 2 wherein one of  $R^1$  and  $R^2$  is hydrogen and the other is  $C_{6-12}$ aryl $C_{1-6}$ alkyl (where the alkyl or aryl moiety may be optionally substituted by one or more ring substituents selected from  $C_{1-6}$ alkoxy and  $C_{2-14}$ heteroaryl);  $R^3$ ,  $R^4$  and  $R^5$  are hydrogen, Y is oxygen, the dotted line represents a bond and  $R^7$  is hydrogen or halogen; or a pharmaceutically acceptable salt or solvate thereof.
- 4. A compound of formula (I) according to any of claims 1 to 3 wherein R<sup>1</sup> and R<sup>2</sup> are both hydrogen; one of R<sup>3</sup> and R<sup>4</sup> is hydrogen and the other is C<sub>1-6</sub>alkyl, C<sub>2-6</sub>alkenyl, C<sub>2-6</sub>alkynyl, C<sub>1-6</sub>alkoxyC<sub>1-6</sub>alkyl or C<sub>6-12</sub>arylalkyl R<sup>5</sup> is hydrogen, Y is oxygen or -NCH<sub>3</sub>, the dotted line represents a bond and R<sup>7</sup> is hydrogen or halogen; or a pharmaceutically acceptable salt or solvate thereof.

- 5 A compound according to claim 1 selected from:
  - 2-(1,2-Benzisoxazol-3-yl)-benzenemethanamine;
  - 2-(1,2-Benzisoxazol-3-yl)-α-2-propenyl-benzenemethanamine;
  - $(R)-(+)-2-(1,2-Benzisoxazol-3-yl)-\alpha-2-propenyl-benzenemethanamine;$
  - (S)-(-)-2-(1,2-Benzisoxazol-3-yl)- $\alpha$ -2-propenyl-benzenemethanamine;
  - 2-(1,2-Benzisoxazol-3-yl)-α-butyl-benzenemethanamine;
  - 2-(1,2-Benzisoxazol-3-yl)-α-2-propynyl-benzenemethanamine;
  - 2-(1-Methyl-IH-indazol-3-yl)- $\alpha$ -2-propenyl-benzenemethanamine;
  - (-)-2-(6-chloro-1,2-benzisoxazol-3-yl)-a-2-propynyl-

benzenemethanamine;

- (S)-(-)-2-(6-chloro-1,2-benzisoxazol-3-yl)-a-2-propenyl-benzene-methanamine;
- and pharmaceutically acceptable salts and solvates thereof.
- 6. A compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof, as defined according to any of claims 1 to 54 for use in therapy.
- 7. Use of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof, as defined according to any of claims 1 to 5, in the manufacture of a medicament for the treatment or prevention of depression.
- 8. Use of a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof, as defined according to any of claims 1 to 5, in the manufacture of a medicament for the treatment or prevention of conditions selected from:
- anxiety disorders, including phobic neuroses, panic neuroses, anxiety neuroses, post-traumatic stress disorder and acute stress disorder;
- attention deficit disorders;
- eating disorders, including obesity, anorexia nervosa and bulimia;
- personality disorders, including borderline personality disorders;
- schizophrenia and other psychotic disorders, including schizo affective disorders, dilusional disorders, shared psychotic disorder, brief psychotic disorder and psychotic disorder;
- narcolepsy-cataplexy syndrome;
- substance related disorders;
- sexual function disorders; and
- sleep disorders.

- 9. A pharmaceutical formulation comprising a compound of formula (I) or a pharmaceutically acceptable salt or solvate thereof, as defined according to claim 1, together with a pharmaceutically acceptable carrier thereof.
- 10. A method for the treatment or prevention of a psychiatric disorder in an animal, which comprises administering to said animal an effective amount of an  $I_h$  channel modulator.
- 11. A method according to claim 10, wherein the psychiatric disorder is depression, anxiety or psychosis.
- 12. A method according to claim 10, wherein the  $I_h$  channel modulator blocks conductance of the  $I_h$  channel and/or the open probability.
- 13. A method according to claim 12, wherein the  $I_b$  channel modulator has a plC50 of 5 to 12 in an  $I_b$  channel modulator functional assay.
  - 14. A compound of formula (I)

$$R_{5}$$
 $R_{2}$ 
 $R_{3}$ 
 $R_{4}$ 

wherein A is a group selected from (a), (b) or (c):

wherein Y is CH or N;

X is O, S, CH=CH, or CH=N;

P and S, which may be the same or different, each represent hydrogen,  $C_{1,4}$ alkyl,  $C_{1,3}$ alkoxy, cyano, halogen, trifluromethyl, phenyl or pyrrole wherein the phenyl or pyrrole moieties may be optionally substituted with halogen or  $C_{1,3}$ alkyl; or P and S together with the ethylene group to which they are bonded form a 1,2-phenylene, a pyridinediyl (including 2,3- and 3,4-pyridinediyl), or a 1-cyclohexen-1,2-diyl group, which groups may be optionally substituted by one or more substituents selected from hydrogen,  $C_{1,4}$ alkyl,  $C_{1,3}$ alkoxy, cyano, halogen, trifluoromethyl, phenyl and pyrrole wherein the phenyl or pyrrole moieties may be optionally substituted with halogen or  $C_{1,3}$ alkyl;

 $R_1$  represents one or more ring substituents selected from hydrogen,  $C_{1:4}$ alkyl,  $C_{1:3}$ alkoxy, cyano, halogen, trifluoromethyl, phenyl and pyrrole wherein the phenyl or pyrrole moieties may be optionally substituted with halogen or  $C_{1:3}$ alkyl;

B is a bivalent radical derived from an aromatic group selected from (d), (e) or (f):

wherein

Z is O or S;

W is O, S or CH=CH,

 $R_1$  is as hereinbefore defined;

R, is NH2;

 $R_3$ ,  $R_4$ , and  $R_5$ , which may be the same or different, each represent halogen,  $C_{14}$ alkyl or hydrogen, or  $R_4$  and  $R_5$  together form a carbon-carbon bond;

n is 0 or 1;

or a physiologically acceptable salt or solvate thereof; with the proviso that when A is group (b) wherein P and S together with the ethylene group to which they are bonded form a 1,2-phenylene group, which group may optionally be substituted by one or more substituents selected from hydrogen, C<sub>14</sub>alkyl, C<sub>13</sub>alkoxy, cyano, halogen, trifluoromethyl, phenyl and pyrrole wherein the phenyl or pyrrole moieties may be optionally substituted with halogen or C<sub>13</sub>alkyl; R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> are as herein before defined and n is 0; then B is a group (e) or (f).

## 15. A compound according to claim 14 of formula (IA)

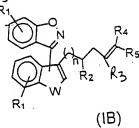
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(IA)

wherein Z,  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$  and  $R_5$  are as defined in claim 14 and n is 0;

or a physiologically acceptable salt or solvate thereof.

16. A compound according to claim 14 of formula (IB)



wherein W,  $R_1$ ,  $R_2$ ,  $R_3$ ,  $R_4$  and  $R_5$  are as defined in claim 14 and n is 0;

or a physiologically acceptable salt or solvate thereof.

17. A compound according to claim 14 of formula (IC)

(IC)

wherein A, R<sub>1</sub>, R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> are as defined in claim 1 and n is 0 or 1, preferably n is 0; or a physiologically acceptable salt of solvate thereof; with the proviso that A is not a group (b) wherein P and S together with the ethylene group to which they are bonded form a 1,2-phenylene group, which group may be optionally substituted by one or more substituents selected from hydrogen, C<sub>14</sub>alkyl, C<sub>13</sub>alkoxy, cyano, halogen, trifluoromethyl, phenyl and pyrrole wherein the phenyl or pyrrole moieties may be optionally substituted with halogen or C<sub>1.3</sub>alkyl; R<sub>2</sub>, R<sub>3</sub>, R<sub>4</sub> and R<sub>5</sub> are as defined in claim 1 and n is 0;

or a physiologically acceptable salt or solvate thereof.

- 18. A pharmaceutical formulation containing a compound of formula (I) or a physiologically acceptable salt or solvate thereof, as defined according to claim 14, together with a pharmaceutically acceptable carrier therefor.
- 19. A method for the treatment or prevention of a psychiatric disorder in an animal, which comprises administering to said animal an effective amount of a compound of formula (I) or a physiologically acceptable salt or solvate thereof, as defined according to claim 14.
- 20. A process for preparing a compound of formula (I) as defined in claim 14 or a physiologically acceptable salt or solvate thereof; which comprises:

## (A) reacting a compound of formula (II)

(II)

wherein A, B,  $R_3$ ,  $R_4$  and  $R_5$  are as defined in claim 1 and  $R_6$  is hydrogen or halogen, with a hydrolysing agent;

(B) reacting an imine of formula (IIA)

(IIA)

wherein A and B are as defined in claim 10, with an appropriate organometallic reagent in the presence of an inert solvent; or

(C) for compounds of formula (I) wherein n is 1, the reduction of a compound of formula (XV)

(XV)

wherein A, B,  $R_3,\ R_4$  and  $R_5$  are as defined in claim 1 and  $R_8$  is an azido group, and

where necessary or desired, following processes A to C above, any one or more of the following further steps in any order may be performed:

- (i) removing any remaining protecting group(s);
- (ii) converting a compound of formula (I) or a protected form thereof into a further compound of formula (I) or a protected form thereof;
- (iii) converting a compound of formula (I) or a protected form thereof into a pharmaceutically acceptable salt or solvate of a compound of formula (I) or a protected form thereof;

  - (v) converting a pharmaceutically acceptable salt or solvate of a compound of formula (I) or a protected form thereof into another pharmaceutically acceptable salt or solvate of formula (I);
  - (vi) where the compound of formula (I) is obtained as a mixture of (R) and (S) enantiomers resolving the mixture to obtain the desired enantiomer;
  - (vii) cleavage of a compound of formula (I) from a solid phase resin.
- 21. A method for identifying compounds useful for the treatment or prevention of psychiatric disorders by measuring the level of  $I_h$  channel modulation in an  $I_h$  channel modulation assay.
- 22. A method for identifying compounds useful for the treatment or prevention of psychiatric disorders by measuring the level of  $I_h$  channel modulation in an  $I_h$  channel modulation assay comprising:
  - taking a brain slice, or a cultured brain slice, or ganglia of the peripheral nervous system, or primary

cell cultures of central and/or peripheral nervous tissue, or cell lines expressing  $I_{\rm h}$  channels incubating and/or exposing these cells and tissues to test compounds and

measuring whether these test compounds affect conductance of the I<sub>b</sub> channel and/or the open probability.